Book Reviews

Molecular Drug Properties: Measurement and Prediction. Edited by Raimund Mannhold. Wiley/VCH, Weinheim, Germany. 2008. xxx + 469 pp. 17 × 25 cm. ISBN 9783527317554. $139.00.

Every drug is a molecule, but every molecule is not a drug—a statement that, despite its obviousness, is underappreciated. What are the physical properties that impart "druglikedness" to a molecule, elevating it from merely being a mundane structure to one that has what it takes to achieve the designation of "drug"? Answering this question is the focus of this very well written and organized monograph. Molecular Drug Properties: Measurement and Prediction is Volume 37 of the popular and successful series Methods and Principles in Medicinal Chemistry. Edited by Raimund Mannhold of the Heinrich-Heine-Universität in Düsseldorf, this volume captures a wealth of theory and pragmatism, from both industry-based and university-based perspectives.

The approaches discussed in this book are primarily in silico with a heavy emphasis on computer-aided drug design techniques for recognizing the molecular properties necessary for druglikedness. However, the material covered is refreshingly different. Most books dealing with computer-aided drug design commence with the mandatory background sections on molecular mechanics, density functional theory, ab initio molecular orbital calculations, and their use in energy minimization calculations at the drug−receptor interface. Mercifully, Molecular Drug Properties: Measurement and Prediction does not revisit this material. Instead, it focuses on the other extremely useful and practical calculations, including lipophilicity, volume of distribution, dissolution properties, solubility, mutagenicity, carcinogenicity, metabolism, toxicity, molecular connectivity indices, and molecular "genotyping". In short, rather than concentrating on the pharmacodynamic phenomena, this book addresses the crucial molecular drug features required for optimal pharmacokinetic and pharmaceutical properties.

For discussions of the molecular drug properties necessary for druglikedness, the book contains 17 chapters logically divided into six sections: Section I provides introductory comments with a focus on physicochemical properties in drug profiling; Section II concentrates on electronic properties with a very interesting chapter on electrotopological state indices; Section III is dedicated to conformational properties; Sections IV and V deal with solubility properties and lipophilicity, respectively; finally, Section VI brings the discussion of a concluding summation with a differentiation between druglikedness and leadlikedness.

Although the focus is on computer-aided drug design, there are a number of very useful sections pertaining to experimental data. For example, there are strong sections on conformational analysis of drugs using nuclear magnetic resonance spectroscopy and on the use of experimental methods (shake-flask method, chromatographic methods) for determining distribution coefficients. These sections nicely complement a book that in general is focused on in silico techniques.

Overall, the book provides a very comprehensive and authoritative approach to presenting the molecular properties necessary for druglikedness, and it does so in a manner that is high in practicality and low in the esoteric information. Many chapters are rich in practical gems. This is particularly true of Lipinski's chapter on drug solubility, which reflects years of industrial experience. His comments on greaseballs, brickdust compounds, salt forms, and amorphous solids are succinct and insightful and will be of use to both novices and veterans of drug design.

In general, the book is written in a concise, easily read manner. The liberal use of frequent subtitles and short, focused bursts of information add to the presentation style. There are no rambling discourses, just the facts. This book both suffers and benefits from its multiauthor format. Although skillful editing has smoothed the reading style, there is a significant degree of variability from chapter to chapter. This is particularly true of the cited references: in some chapters the reference citations are comprehensive; in others they are somewhat sparse. There is also a fair amount of repetition. This is most evident in the discussions of log *P* that permeate many chapters. Although I initially thought that this was an annoying weakness, by the end of the book I appreciated the different perspectives brought to similar topics by different authors, and there are many authors, 35 in total, 14 of whom are from industrial laboratories. The presentation style would also have benefited from a greater use of figures and diagrams, especially color figures (although regrettably at the cost of increased price).

Molecular Drug Properties: Measurement and Prediction is a good read and a useful book and will provide valuable advice to the ever increasing diversity of researchers tackling the task of drug design.

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Arrow Pushing in Organic Chemistry: An Easy Approach to Understanding Organic Reaction Mechanisms. By Daniel E. Levy. John Wiley & Sons, Hoboken, NJ. 2008. xv + 301 pp. 18 × 25.5 cm. ISBN 978-0-470-17110-3. $39.95.

Arrow Pushing in Organic Chemistry joins a growing number of supplemental guides intended to assist students to attain mastery of undergraduate organic chemistry. The 300-page monograph is predominantly a workbook. Eight short chapters, which are generously illustrated, are followed by groups of practice problems laid out in workbook style; detailed solutions are provided in an appendix.

The first three chapters introduce arrow-pushing electron flow, bonding, acids, and bases. Chapters 4−6 focus on substitution and elimination. The repeated misuse of examples of E1cb reactions to illustrate E2 elimination will confuse students struggling to understand reaction order or stereoelectronics.

Chapter 7 is an overview of additions to alkenes and carbonyls, mechanistically distinct topics separated by a semester in most organic sequences. (Concerns with order of presentation crop up elsewhere; inexperienced readers will be intimidated by the illustration of Wittig, aldol, Diels−Alder, and tin hydride reactions in Chapter 1). The textual material on alkene addition is limited to bromination and hydrohalogenation. The description of alkene protonation as involving a three-atom, two-electron

intermediate conflicts with a later description of hyperconjugation and will confuse students on how and when bonding of hydrogen can exceed a duet. Additions to aldehydes and ketones are illustrated for organometallics and cyanide; examples of oxime/imine/enamine, aldol, Wittig, and related chemistries are included in the problems. Addition/elimination reactions of carboxyl derivatives are illustrated but without any textual discussion of relative reactivity. The eighth and final chapter, entitled "Moving Forward", mentions a number of name reactions and functional group manipulations; in many cases, details are found only within the solved problems.

The philosophy underpinning this monograph, that a better command of fundamental mechanistic concepts will help students identify patterns of organic reactivity, is an attractive one. However, the idea that a mechanistically based approach will minimize the need for memorization is oversimplified. Organic chemistry is a challenging course for many students precisely because it requires mastery of a new symbolic logic (organic mechanisms and transformations) applied within the new "language" of organic structure and bonding. Overall, this book gathers and presents basic mechanistic information relevant to a second year organic chemistry course. Some common failings of traditional texts are also found here, including inconsistent use of equilibrium and resonance arrows and omission of separate steps for proton transfers and dehydrations. The most valuable materials in the book are the many solved problems; however, the accessibility and utility of these problems will be limited by the shortcomings of the gatekeeper chapters.

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